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Patents and Trademarks

December 5, 2007

Mail Stop Appeal Brief - Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Re: Response to Notification of  
Non-Compliant Appeal Brief  
Serial No.: 10/687,788  
Filed: October 17, 2003  
For: SAMPLE FOR MANIPULATION BY AN OPTICAL  
TWEezer AND A MEHTOD AND DEVICE TO GENERATE  
OPTICALLY INDUCED FORCES  
Our ref: SHA-001 (Shamci Monajembashi)

Dear Sir or Madam:

In compliance with the "Notification of Non-Compliant Appeal Brief" mailed November 5, 2007 from the Patent and Trademark Office regarding the above-identified patent application, enclosed is Applicant-Appellant's Amended Appeal Brief.

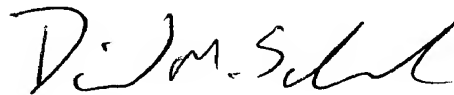
CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) on the date shown below.

Signed: Sally Azevedo  
Typed Name: Sally Azevedo

Date: December 5, 2007

Respectfully submitted,



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant: Shamci Monajembashi PATENT APPLICATION  
Serial No: 10/687,788 Group Art Unit: 1631  
Filed: October 17, 2003 Examiner: Mr. Pablo S. Whaley  
Confirmation No.: 9873 Attorney Docket No.: SHA-001  
For: SAMPLE FOR MANIPULATION BY AN OPTICAL TWEEZER, AND A  
METHOD AND DEVICE TO GENERATE OPTICALLY INDUCED FORCES

Applicant-Appellant's Amended Brief

Introduction

This is an amended appeal brief under 37 C.F.R. 41.37 relating to the rejection of claims 16-19, 21, 24-26, 28, and 29 in the above-identified patent application. The fee for filing this appeal brief was paid electronically. Please charge any additional fee to Deposit Account No. 19-0590.

(i) *Real Party in Interest.* This patent application has not been assigned; the real party in interest is the inventor, Dr. Shamci Monajembashi.

(ii) *Related Proceedings.* There are no related appeals, interferences or judicial proceedings known to Applicants-Appellants.

(iii) *Status of Claims.* Claims 16-19, 21, 24-26, 28 and 29 are rejected. Claims 1-15 and 27 are withdrawn. Claims 20, 22, and 23 are cancelled. The rejection of claims 16-19, 21, 24-26, 28 and 29 is appealed.

(iv) *Status of Amendments.* A Response After Final Rejection to the claims and specification dated June 15, 2007 was filed after the final rejection. Although the Advisory Action states that the amendments to the claims would not be entered (Box 7a of the Advisory Action), the Applicant respectfully notes that no amendments were made in this Response After Final Rejection. The pending claims are those examined and rejected in the most recent Office action.

(v) *Summary of Claimed Subject Matter.* Applicant's-Appellant's claim in independent claim 16 a method for producing optically

induced mechanical forces on a target cell (Fig. 1, 2; Specification at page 12, line 9 to page 13, line 10), comprising adhering to at least one target cell at least one auxiliary object selected from a group consisting of erythrocytes, haemoglobin, a haemoglobin derivative, a chromophore and a chloroplast (page 4 line 24 to page 5 line 18, page 7, lines 1-14), and applying an optical tweezer to said auxiliary wherein said mechanical forces are induced to said target cell by application of the optical tweezer to said auxiliary object (Fig. 1, 2; Specification at page 12, line 9 to page 13, line 10.)

Applicants-Appellants claim in independent claim 21 a system for including optical forces for manipulating a target cell (Figures 3 and 4, page 13, line 11 to page 14, line 35), comprising an optical tweezer (Figure 3, element 17, page 13, lines 11-19) including a laser beam (Figure 3, element OP, page 13, lines 17-18) with a focus (Figure 1, element 15, page 12, lines 17-20), a microscope having a beam passage (Figures 3 and 4, page 13, line 11 to page 14, line 35) and a target cell (Figure 1, element 11, page 12, lines 9-13) an adherent auxiliary object aligned with said laser beam (Figure 1, element 12, page 12, lines 11-13), wherein said laser beam and said beam passage are coupled together for manipulating the target cell toward said focus, wherein said auxiliary object is selected from a group consisting of erythrocytes, haemoglobin, a haemoglobin

derivative, a chromophore and a chloroplast (page 4 line 24 to page 5 line 18, page 7, lines 1-14)

(vi) *Grounds of Rejection to be Reviewed on Appeal.*

1) whether claims 16-19 are unpatentable under 35 U.S.C. § 103 over Henon et al. in view of Jan et al.;

2) whether claims 16-19 are unpatentable under 35 U.S.C. § 103 over Visscher et al. in view of Jan et al. and Shaw et al.

3) whether claims 21, 24-26, 28, and 29 are unpatentable under 35 U.S.C. § 103 over Henon et al. in view of Jan et al.; and

4) whether claims 21, 24-26, 28, and 29 are unpatentable under 35 U.S.C. § 103 over Visscher et al. in view of Jan et al.; and Shaw et al.

(vii) *Argument.*

In the most recent Advisory Action, the rejection of claim 18 as indefinite under 35 USC § 112 has been withdrawn. The sole remaining issue is whether the pending claims 16-19, 21, 24-26, 28 and 29 are rendered obvious by the cited references.

Claims 16-19

Claims 16-19 are method claims, claim 16 and independent method claim and claims 17-19 dependent on independent claim 16. These claims stand or fall together.

In making an obviousness rejection, the Examiner must first determine the scope and content of the prior art, ascertain the differences between the prior art and the claims in issue, and resolve the level of ordinary skill in the art. Graham v. John Deere 148 USPQ 459 (1966). In order to establish a *prima facie* case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 180 USPQ 580 (CCPA 1974). Under these standards the present claims are not obvious.

Henon and Jan fail to teach the elements of claims 16-19.

Claims 16-19 were found obvious under Henon et al. ("Henon hereafter") in view of Jan et al. ("Jan" hereafter). Henon is cited for a number of elements claimed in independent claim 16, but the Office action acknowledges, "Henon et al. do not specifically teach adhering erythrocytes to "target cells." Instead this reference merely notes that the geometry of red blood cells can be altered. The Office action then fails to cite anything from the second reference to teach this missing claim element. Nothing in Jan et al. teaches adhering to at least one target cell at least one auxiliary object, such as an erythrocyte. Instead, the second reference is cited as "Jan et al. teach methods for analyzing the role of surface electric charge in red blood cell interactions wherein erythrocytes (e.g., auxiliary cells) are coated with substances that change the surface charge of the erythrocyte". What the examiner has ignored is that this teaching is to prevent erythrocyte adhesion, rather than to use erythrocytes as an adherent auxiliary object, as claimed by the Applicants. This teaching would lead a person of ordinary skill in the art to conclude that the method of the present claim should not be practiced. The Applicant also notes that the alternative auxiliary objects, including haemoglobin,

haemoglobin derivatives, chromophore or chloroplasts are also not disclosed in either of the cited reference.

Claims 16-19 are not obvious because there is not proper teaching to combine Henon with Jan.

In addition to failing to teach the claimed elements, there is no proper cited teaching to combine the two cited references. One of the basic requirements of a prima facie case of obviousness is that some teaching to combine the references must be preferred. See MPEP § 2143. In the recent KSR Int'l Co. v. Teleflex Inc. decision, the Supreme Court found:

"a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combining the elements in the way the claimed new invention does". 550 US \_\_\_\_\_ (2007). The Federal Circuit has established that if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the reference are not sufficient to render the claims obvious. In re Ratti, 123 USPQ 349 (CCPA 1959).

The motivation to combine the references as cited in the Office action is: "it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to adhere chemically aggregated erythrocytes taught by Jan et al. with bead bound erythrocytes using the optical using the optical tweezer method and system of Henon et al., where the motivation would have been a clinical interest in developing improved methods for inhibiting blood cell aggregation [Jan et al. abstract]." However, Jan et al. actually state that their "present experiments were designed to study the role of RBC surface charge in affecting the effectiveness of dextrans . . . in inducing RBC aggregation." Jen, p. 638. Rather than inhibiting aggregation, as the Office action suggests, Jan et al. actually examine the induction of RBC aggregation. This stands in contrast to the incompatible teachings of Henon, which is a study of erythrocyte membrane elasticity. Such a study requires free erythrocytes in suspension rather than adherent cells. The very notion that an experimenter would adhere aggregated erythrocytes by a motivation to inhibit blood cell aggregation does not make logical sense. This appears to state that one would clump cells together motivated by a desire not to clump cells together. The presented reason indicates that the two cited references teach at cross-purposes and would not be combined to reach the applicants claims. This provides a second, independent reason to reconsider the present rejections.

Visscher in view of Jan and Shaw also do not render obvious Applicant's claims 16-19.

Next, claims 16-19, were found rendered obvious by Visscher et al. ("Visscher" hereafter) in view of Jan and Shaw et al. ("Shaw" hereafter). Again, the rejections of record are not sufficient to make a prima facie showing of obviousness.



Visscher et al. have developed a micromanipulator employing multiple optical traps created by a single beam. This is demonstrated using bacterial cells that are directly trapped. On page 113, the authors also note that indirect trapping is possible using beads. In one such example, the beads are coated with monoclonal antibodies. Visscher et al. does not teach adhering a target cell to an erythrocyte. Jan et al. also does not teach adhering a target cell to an erythrocyte to a target cell, but instead merely explores conditions under which red blood cells aggregate together. Shaw et al. also do not teach this lacking claim element. Given that at least one element of claim 16, namely adhering a target cell and an auxiliary object such as an erythrocyte, is not found in the cited reference this combination of references does not render the applicant's claim 16 obvious.

There is no teaching to combine Visscher with Jan and Shaw. In addition to failing to teach the claimed elements, there is no proper cited teaching to combine the two cited references. One of the basic requirements of a prima facie case of obviousness is that some teaching to combine the references must be preferred. See MPEP § 2143. In the recent KSR Int'l Co. v. Teleflex Inc. decision, the Supreme Court found:

"a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to their established functions, it can be important to identify a reason that would have prompted a person of ordinary

skill in the relevant field to combining the elements in the way the claimed new invention does". 550 US \_\_\_\_\_ (2007). The Federal Circuit has established that if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the reference are not sufficient to render the claims obvious. In re Ratti, 123 USPQ 349 (CCPA 1959).

In addition to failing to teach all of the claimed elements, the present Office action also does not cite a proper teaching to combine the references. Visscher does not require modification to allow application of pressure to a cell because a bead is already disclosed for this purpose. Given that a this reference already teaches a technology to apply forces to cells there would be no motivation to adopt the claimed use of auxiliary objects. The cited references actually teach away from the claimed combination. This provides another independent reason to reconsider the instant rejection.

Henon and Jan fail to teach the elements of claims 21, 24-26, 28 and 29.

Independent apparatus claim 21 and dependent claims 24-26, 28, 29 also stand or fall together.

With respect to claim 21, the Office action again fails to disclose, in either Henon or Jen references, a target cell and an adherent auxiliary object, such as an erythrocyte. This system requires an adherent auxiliary object, such as an erythrocyte, that is aligned with the laser beam. Not only is this not disclosed in the cited reference, Henon et al. actually would lead to development of a system that precluded the claimed system target. The cited reference requires aligning the beam not with

the red blood cells but instead with beads, which are not a claimed auxiliary object.

In the present patent claims, the applicant has recognized that red blood cells and other auxiliary objects are superior to beads as force transducers for axial deformation (i.e. a force with direction into the cell or way from it surface.) The auxiliary objects have a chromophore allowing the object to be used as a force transducer and force amplifier. This can be contrasted with Henon et al., a reference that teaches the to apply force to cells via beads. As is repeatedly stressed in Henon et al., force is applied to the beads, not the red blood cells, for moving the cells. This is the exact opposite of what is claimed, using cells as the auxiliary object onto which the force is directed.

Claims 24-26, and 28 each depend from claim 21 and should be found allowable for at least the same reasons claim 21 is allowable.

No Teaching to Combine Henon and Jan.

As noted above, the teachings of Henon and Jan are not required modification of the references that is at cross purposes with the references. This lack of a proper teaching to combine provides a second independent reason that the two references could not be combined.

Visscher in view of Jan and Shaw also do not render obvious Applicant's claims 21, 24-26, 28, and 29.

Claims 21, 24-26, 28, and 29 were found rendered obvious by Visscher in view of Jan and Shaw. Again, the Applicant respectfully disagrees with this finding.

As noted Visscher developed a micromanipulator employing multiple optical traps created by a single beam. This is demonstrated using bacterial cells that are directly trapped. On page 113, the authors also note that indirect trapping is

possible using beads. In one such example, the beads are coated with monoclonal antibodies. Visscher does not teach adhering a target cell to an erythrocyte. Jan also does not teach adhering a target cell to an erythrocyte to a target cell, but instead merely explores conditions under which red blood cells aggregate together.

Claim 21 is directed to a system including a target cell and an adherent auxiliary object such as an erythrocyte. As already noted, none of the cited references teach this element. Instead, Visscher teach away from this element by disclosing that it already has a preferred method of moving target cells, namely using beads as an auxiliary object.

Claims 24-26, and 28 depend on claim 21. For at least the same reason claim 21 is allowable, claims 24-26, and 28 should also be allowed.

No Teaching to Combine Visscher with Jan and Shaw.

As noted above, the teachings of Visscher, Jan, and Shaw are not required modification of the references that is at cross purposes with the references. This lack of a proper teaching to combine provides a second independent reason that the two references could not be combined.

## Conclusion

Applicant-Appellant submits that the Examiner has failed to establish a prima facie case of obviousness for the pending claims. Reversal of the rejection of claims 16-19, 21, 24-26, 28, and 29 is respectfully requested.

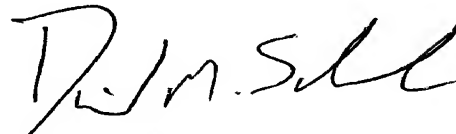
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Signed:   
Typed Name: Sally Azevedo

Date: December 5, 2007

Respectfully submitted,



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(vii) *Claims Appendix*. An appendix containing a copy of the claims involved in the appeal.

1. (Withdrawn) A sample for manipulation by an optical tweezer, comprising one or more target objects and one or more auxiliary objects, at least one auxiliary object being linked to at least one target object, wherein the at least one auxiliary object includes haemoglobin or a haemoglobin derivate.

2. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects includes a haemoglobin like protein body.

3. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects includes muscle haemoglobin.

4. (Withdrawn) The sample of claim 3 wherein said muscle haemoglobin is myoglobin.

5. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects has a biconcave form.

6. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects has a round form.

7. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects has a thorn apple form.

8. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects is a red blood cell.

9. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects is a liposome containing haemoglobin or a haemoglobin derivate.
10. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects is a colloidal polymer microcapsule.
11. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects includes a coating comprising a substance, the surface charge of which is opposite the surface charge of the target object.
12. (Withdrawn) The sample of claim 11 wherein said substance includes positively charged polymers, which do not show any reactive groups.
13. (Withdrawn) The sample of claim 1 wherein said one or more auxiliary objects has a poly-ethylene-imide or poly-L-lysine coating.
14. (Withdrawn) The sample of claim 1 wherein said one or more target objects is a biological cell.
15. (Withdrawn) The sample of claim 1 wherein said one or more target objects is fixed on a carrier and said one or more auxiliary objects is fixed on said one or more target objects.

16. A method for producing optically induced mechanical forces on a target cell comprising:

adhering to at least one target cell at least one auxiliary object selected from a group consisting of erythrocytes, haemoglobin, a haemoglobin derivate, a chromophore and a chloroplast; and

applying an optical tweezer to said auxiliary object wherein said mechanical forces are induced to said target cell by application of the optical tweezer to said auxiliary object.

17. The method of claim 16 further comprising coating said at least one auxiliary object, before adhering, with substances which change a surface charge such that the target cell and the at least auxiliary object show surface charges with differing signs.

18. The method of claim 16 wherein said auxiliary object is a fixed erythrocyte.

19. The method of claim 16 wherein said optical tweezer includes one or more optical beams.

20. (Cancelled)



21. A system for inducing optical forces for manipulating a target cell, comprising:

an optical tweezer including a laser beam with a focus;  
a microscope having a beam passage; and

a target cell and an adherent auxiliary object, aligned with said laser beam, wherein said laser beam and said beam passage are coupled together for manipulating the target cell toward said focus, wherein said auxiliary object is selected from a group consisting of erythrocytes, haemoglobin, a haemoglobin derivate, a chromophore and a chloroplast.

22-23. (Cancelled)

24. The system of claim 21 wherein said optical tweezer includes multiple laser beams.

25. The system of claim 24 further comprising optical elements forming multiple laser beams.

26. The system of claim 21 wherein said laser beam is a longwave laser beam.

27. (Withdrawn) The system of claim 21 wherein said laser beam is coupled directly into said beam passage.

28. The system of claim 21 wherein said laser beam is coupled into said beam passage via a system of lenses.

29. The system of claim 21 wherein said microscope is a confocal laser scanning microscope.

(ix) *Evidence Appendix.*

Non-patent documents: Henon et al. Biophysical Journal, 1999, Vol. 76, pp. 1145-1151; Visscher et al., Cytometry, 1993, Vol. 14, pp. 105-114; Jan et al., The Journal of General Physiology, 1973, vol. 61, pp. 638-654; and Shaw et al. Cellular Microbiology, 2001, Vol. 3, No. 4, pp. 213-222.

These documents were relied upon by the Examiner as to grounds of rejection to be reviewed on appeal. Copies of the documents are attached herewith.

(x) *Related Proceedings Appendix.*

None.